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10/586,107	07/14/2006	Giampiero De Luca	30694/39646B	1782

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EXAMINER	
CHANDRA, GYAN	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
10/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,107	DE LUCA, GIAMPIERO	
	Examiner	Art Unit	
	GYAN CHANDRA	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/30/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 6/30/2008 is acknowledged and fully considered.

Status of Application, Amendments, And/Or Claims

The amendments of claims 1-3, 6-10, 12, 14 and 15 and the cancellation of claims 18-24 have been made of record.

Claims 1-17 are pending and under examination.

Response to Arguments

Claim Objections-withdrawn

The objection to claim 1 for reciting the term "a human suffering from" because the method is drawn to treating a disease rather than treating a human suffering is withdrawn in view of applicant's amendments of claim 1 to a method of treating lipodystrophy.

Claim Objections

Claims 11 and 13 are objected to because of the following informalities:

In claim 11, the term "diabetes related" should be hyphenated.

The Examiner suggests that syntax of claim 13 can be improved by replacing the term "is suffering from" with "has diabetes."

Appropriate correction is required.

Claim Rejections - 35 USC § 102-*maintained*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 remain rejected under 35 U.S.C. 102(b) as being anticipated by Rudling et al (IDS, WO 00/23097).

Claims 1-8 are broadly drawn to a method of treating lipodystrophy, the method comprising administering to a human having said disorder a growth hormone and a statin-based therapeutic agent (claim 1), wherein statin-based therapeutic agent and said growth hormone is provided in a single pharmaceutical composition (claim 2), wherein said statin-based therapeutic agent is provided in a first pharmaceutical composition and said growth hormone is provided in a second pharmaceutical composition (claim 3), wherein said growth hormone is recombinant growth hormone (claim 4), wherein said growth hormone is isolated from an animal (claim 5), wherein said statin-based agent is a lovastatin or a lovastatin analog (claim 6), wherein said statin-based therapeutic agent is selected from the group consisting of atorvastatin, pravastatin, simvastatin, lovastatin, and fluvastatin (claim 7) and wherein said lipodystrophy is non-HIV-related lipodystrophy (claim 8).

Applicants argue (page 6 of Response) that the reference Rudling et al teaches treating familial hypercholesterolemia but not lipodystrophy as recited in the amended claims. Applicants provide Harrison's Principles of Internal Medicine 2249, and

Lichtesntein et al. (2001) to support that the term "lipodystrophy" being a syndrome caused by a deficiency and/or destruction of adipocytes and characterized by an abnormal distribution of adipose tissue. Additionally, Applicants argue that lipodystrophy may be associated with hypertriglyceridemia, hyperlipidemia, hepatic steatosis, and insulin resistance but hypercholesterolemia is simply not the same symptom as lipodystrophy, and they provide the reference Rakotambinina et al in support of their arguments.

Applicants' arguments have been fully considered but they are not persuasive for the reasons of record in pg. 3-5 of the Office Action of 4/1/2008 and because the instant claims do not require a subject having lipodystrophy. Therefore, the reference Rudling et al which teaches administering GH or analogues thereof, optionally in combination with established lipid-lowering treatment to mammals with high plasma cholesterol (page 4, 1st paragraph and Detailed description of the invention and claim 1) inherently anticipates the instant invention. Regarding the cited reference Lichtenstein, it is noted that the reference primarily focuses on the relationship between lipodystrophy and antiretroviral therapy and that the reference Lichtenstein does not disclose any relationship between lipodystrophy and growth hormone or the therapeutic agents, statins as instantly claimed. Furthermore, the instant claims do not require said subject to have lipodystrophy. It is noted that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand

alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Therefore, the rejection is maintained. To overcome this rejection, Applicant could amend the claim to include the term "in need thereof" after the word "subject" in line 3 of claim 1. However, this will amendment not necessarily preclude a rejection of these claims under 35 USC 103.

Claim Rejections - 35 USC § 103-*maintained*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rudling et al (IDS, WO 00/23097) as applied to claims 1-8 above, and further in view of Carr (IDS, AIDS, vol. 17: S141-S148, 2003).

The instant claims are drawn to a method of treating lipodystrophy comprising administering to a subject a growth hormone and a statin-based therapeutic agent, wherein said lipodystrophy is HIV-related lipodystrophy, wherein said HIV-related lipodystrophy is selected from the atherogenic dyslipidemia, hypertriglyceridemia, elevated levels of cholesterol, elevated levels of LDL cholesterol, or low level of HDL cholesterol, wherein said subject manifests a symptom associated with diabetes related adiposity, wherein said symptom is selected from the group consisting of insulin

resistance, beta-cell dysfunction (claim 12), and wherein said subject is suffering from Type 2 diabetes (claim 13).

Applicants argue (page 7 of Response) that the reference Carr only teaches to use statins in the context of lowering lipids and not in the context of treating lipodystrophy. Applicants argue that the combined references do not establish that one of skill in the art would have a reasonable success in treating lipodystrophy. Applicants argue (page 14) that metformin is not an insulin secretagogue and provides Monami et al (2006) in support.

Applicants' arguments have been fully considered but they are not persuasive for the reasons of record in pages 5-8 of the office action of 4/1/2008 and as discussed below. The teachings Rugling et al are summarized as set forth above. Carr et al teach that lipodystrphy occurs in patients infected with HIV and they describe that the main clinical features in these subjects are peripheral lipoatrophy of the face, limbs and buttucks, and cetral fat accumulation (within the abdomen, breasts and over the deno-cervical spine [so –called "buffallo hump"]) (pg. S141, 1st paragraph). Further, Carr et al teach that insulin resistance, type 2 diabetes, hypertriglyceridemia and hypercholesterolemia are significantly associated with lipodystrophy. Therefore, one of skill in the art would combine a treatment (such as metformin or thiazolidinediones [see talble 2]) as taught by Carr et al that would treat type 2 diabetes and insulin resistance along with GH and statins. Applicants' arguments that metformin is not an insulin secretagogue has been fully considered and are found persuasive. However, inclusion of claim 14 in this rejection was a typographical error as claim 14 is rejected over the

reference Van Gall and Leeuw (see page 8 of the previous office action mailed on 4/1/2008) and therefore, arguments are addressed below.

Claims 14-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rudling et al in view of Carr et al as applied to claims 1-13 above, and further in view of Van Gaal and Leeuw (Diabetologia, 46: M44-M50, 2003).

The instant claims are drawn to a method of treating an abnormal lipid distribution disorder comprising administering to a human having said disorder a growth hormone and a statin-based therapeutic agent, wherein said subject is further treated with an insulin secretagogue (claim 14), wherein a secretagogue is selected from the group consisting of sulfonyl urea, glyburide....., and exendin-4 (claim 15), and wherein said insulin secretagogue is a non-glucose dependent insulin secretagogue and wherein administering said GH, statin and insulin secretagogue produces insulin release patterns capable of attaining glucose dependent, bi-phasic release characteristics with reduced likelihood of producing hypoglycemia (claim 16).

Applicants argue (page 8 of Response) that the reference Van Gaal and Leeuw does not cure the deficiency of Rudling et al and Carr because the reference treats treating diabetes which is not a lipid distribution disorder (i.e., lipodystrophy). They argue that the combined references do not teach or suggest a method for treating lipodystrophy using a GH and a statin-based thereapeutic agent.

Applicants' arguments have been fully considered but they are not persuasive because Carr et al characterize lipodystrophy in a subject as having peripheral

lipoatrophy of the face, limbs and buttucks, and central fat accumulation (within the abdomen, breasts and over the deno-cervical spine [so –called "buffallo hump"]) (pg. S141, 1st paragraph). They teach that insulin resistance, type 2 diabetes, hypertriglyceridemia and hypercholesterolemia are significantly associated with lipodystrophy. Rudling et al teach administering compounds selected from GH, analogues thereof, optionally in combination with established lipid-lowering treatment to mammals with high plasma cholesterol (page 4, 1st paragraph and Detailed description of the invention and claim 1). They teach that the lipid lowering drug can be a statin. Therefore, it would be obvious to one of the skill in the art to treat lipodystrophy by combining a GH, a statin and an insulin secretagouge as taught by Van Gall and Leeuw. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Claim 17 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Rudling et al (IDS, WO 00/23097) as applied to claims 1-8 above, and further in view of Oral et al (N. Eng. J. Med. 346: 570-578. 2002).

The instant claims are drawn to a method of treating an abnormal lipid distribution disorder comprising administering to a human having said disorder a growth

hormone and a statin-based therapeutic agent, wherein said subject is further treated with leptin.

Applicants argue (pg. 8-9 of Response) that the reference Rudling et al teach administering a GH and a statin for treating hyercholesterolemia and not to treat lipodystrophy which is a different clinical disorder. Therefore, the teachings of Oral et al does not cure the deficiencies of Rudling et al. Applicants argue that the office does not provide a reason to combine the references Rudling et al and Oral et al and that the office does not establish a reasonable expectation of success in combining the references.

Applicants' arguments have been fully considered but they are not persuasive for the reasons of record in pg. 10-11 of the office action of 4/1/2008 and because Oral et al teach that lipodystrophy is caused by a deficiency or destruction of adipose tissues which results in conditions including insulin resistance a hypertriglyceridemia (page 570, right column). Oral et al teach that the administration of leptin reduces triglyceride and treats lipodystrophy (pg. 570, Discussion). Applicants' arguments that the office does not provide a reason to combine the reference have been fully considered but they are not deemed persuasive because Oral et al teach that the risk factors such as hypertriglyceridemia and insulin resistance are associated with lipodystrophy; and Rudling et al also teach that risk factors such as hypercholesteremia to be treated by a GH and a statin. Therefore, in order to have an additive effect over either single treatment (GH or a statin), one skilled in the art would have combined these treatments. Further, Applicants arguments that the offices does not establish a reasonable

expectation of success in combining the references have been fully considered but they are not persuasive because Oral et al teach administering leptin to treat hypertriglyceridemia and insulin resistance which is well known in the art to be associated with hypercholesterolemia, therefore, one skilled in the art would have success in combining leptin with the treatment of Rudling et al for additional response.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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